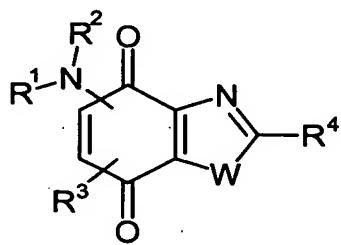


Claims

1. Product comprising at least one Cdc25 phosphatase inhibitor in combination with at least one other anti-cancer agent for a therapeutic use which is simultaneous, separate or spread over time in the treatment of cancer.
- 5 2. Product according to claim 1, characterized in that the Cdc25 phosphatase inhibitor combined with the other anti-cancer agent is a compound of general formula (I)



(I)

in which:

10  $R^1$  represents a hydrogen atom or an alkyl, alkoxyalkyl, alkylthioalkyl, cycloalkyl,  $-(CH_2)-X-Y$ ,  $-(CH_2)-Z-NR^5R^6$  radical or a  $-CHR^{35}R^{36}$  radical in which  $R^{35}$  and  $R^{36}$  form together with the carbon atom which carries them an indanyl or tetralinyl radical, or also  $R^{35}$  and  $R^{36}$  form together with the carbon atom which carries them a saturated heterocycle containing 5 to 7 members and 1 to 2 heteroatoms chosen from O, N and S, the nitrogen atoms of said heterocycle being optionally substituted by radicals chosen from the alkyl radicals and the benzyl radical,

15  $R^1$  also being able, when  $W$  represents O, to represent moreover a carbocyclic aryl radical optionally substituted 1 to 3 times by substituents chosen independently from a halogen atom and an alkyl, haloalkyl or alkoxy radical,

X representing a bond or a linear or branched alkylene radical containing 1 to 5 carbon atoms,

20 Y representing a saturated carbon-containing cyclic system with 1 to 3 condensed rings chosen independently from rings with 3 to 7 members, or Y representing a saturated heterocycle containing 1 to 2 heteroatoms chosen independently from O, N and S and attached to the X radical by an N or CH member, said saturated heterocycle moreover

containing 2 to 6 additional members chosen independently from  $-\text{CHR}^7-$ ,  $-\text{CO}-$ ,  $-\text{NR}^8-$ ,  $-\text{O}-$  and  $-\text{S}-$ ,  $\text{R}^7$  representing a hydrogen atom or an alkyl radical and  $\text{R}^8$  representing a hydrogen atom or an alkyl or aralkyl radical, or also  $\text{Y}$  representing a carbocyclic or heterocyclic aryl radical optionally substituted 1 to 3 times by substituents chosen independently from the group constituted by a halogen atom, an alkyl radical, a haloalkyl radical, an alkoxy radical, a haloalkoxy radical, a hydroxy radical, a nitro radical, a cyano radical, the phenyl radical, an  $\text{SO}_2\text{NHR}^9$  radical and an  $\text{NR}^{10}\text{R}^{11}$  radical,  $\text{R}^9$  representing a hydrogen atom or an alkyl or phenyl radical, and  $\text{R}^{10}$  and  $\text{R}^{11}$  independently representing alkyl radicals,

10  $\text{Z}$  representing a bond or a linear or branched alkylene radical containing 1 to 5 carbon atoms,  $\text{R}^5$  and  $\text{R}^6$  being chosen independently from a hydrogen atom, an alkyl, aralkyl or  $-(\text{CH}_2)_n\text{OH}$  radical in which  $n$  represents an integer from 1 to 6, or  $\text{R}^5$  representing an alkoxy carbonyl, haloalkoxy carbonyl or aralkoxy carbonyl radical and  $\text{R}^6$  representing a hydrogen atom or a methyl radical,

15 or also  $\text{R}^5$  and  $\text{R}^6$  forming together with the nitrogen atom a heterocycle with 4 to 7 members comprising 1 to 2 heteroatoms, the members necessary to complete the heterocycle being chosen independently from the  $-\text{CR}^{12}\text{R}^{13}-$ ,  $-\text{O}-$ ,  $-\text{S}-$  and  $-\text{NR}^{14}-$  radicals,  $\text{R}^{12}$  and  $\text{R}^{13}$  representing independently each time that they occur a hydrogen atom or an alkyl radical, and  $\text{R}^{14}$  representing a hydrogen atom or an alkyl or aralkyl radical, or also  $\text{R}^{14}$  representing a phenyl radical optionally substituted 1 to 3 times by substituents chosen independently from a halogen atom and an alkyl or alkoxy radical,

20  $\text{R}^2$  representing a hydrogen atom or an alkyl or aralkyl radical;

25 or also  $\text{R}^1$  and  $\text{R}^2$  forming together with the nitrogen atom a heterocycle with 4 to 8 members comprising 1 to 2 heteroatoms, the members necessary to complete the heterocycle being chosen independently from the  $-\text{CR}^{15}\text{R}^{16}-$ ,  $-\text{O}-$ ,  $-\text{S}-$  and  $-\text{NR}^{17}-$  radicals,  $\text{R}^{15}$  and  $\text{R}^{16}$  independently representing each time that they occur a hydrogen atom or an alkyl radical, and  $\text{R}^{17}$  representing a hydrogen atom or an alkyl or aralkyl radical;

30  $\text{R}^3$  represents a hydrogen atom, a halogen atom, or an alkyl, haloalkyl, alkoxy or alkylthio radical;

$\text{R}^4$  represents an alkyl, cycloalkyl, cycloalkylalkyl, cyano, amino,  $-\text{CH}_2\text{COOR}^{18}$ ,  $-\text{CH}_2\text{CO-NR}^{19}\text{R}^{20}$  or  $-\text{CH}_2\text{NR}^{21}\text{R}^{22}$  radical, or  $\text{R}^4$  represents a carbocyclic or heterocyclic aryl radical optionally substituted 1 to 4 times by substituents chosen independently from a halogen atom and an alkyl, haloalkyl, alkoxy,

haloalkoxy or  $NR^{37}R^{38}$  radical, or also  $R^4$  represents a phenyl radical possessing two substituents which form together a methylenedioxy or ethylenedioxy radical,  
5  $R^{18}$  representing a hydrogen atom or an alkyl radical,  
 $R^{19}$  representing a hydrogen atom, an alkyl radical or an aralkyl radical the aryl group of which is optionally substituted 1 to 3 times by substituents chosen independently from the group constituted by a halogen atom, an alkyl radical, a haloalkyl radical, an alkoxy radical, a haloalkoxy radical, a hydroxy radical, a nitro radical, a cyano radical, the phenyl radical, an  $SO_2NHR^{23}$  radical and an  $NR^{24}R^{25}$  radical,  $R^{23}$  representing a hydrogen atom or an alkyl or phenyl radical, and  $R^{24}$  and  $R^{25}$  independently representing alkyl radicals,  
10  $R^{20}$  representing a hydrogen atom or an alkyl radical,  
or also  $R^{19}$  and  $R^{20}$  forming together with the nitrogen atom a heterocycle with 4 to 7 members comprising 1 to 2 heteroatoms, the members necessary to complete the heterocycle being chosen independently from the  $-CR^{26}R^{27}$ -,  $-O-$ ,  $-S-$  and  
15  $-NR^{28}-$  radicals,  $R^{26}$  and  $R^{27}$  independently representing each time that they occur a hydrogen atom or an alkyl radical, and  $R^{28}$  representing a hydrogen atom or an alkyl or aralkyl radical, or also  $R^{28}$  representing a phenyl radical optionally substituted 1 to 3 times by substituents chosen independently from a halogen atom and an alkyl or alkoxy radical,  
20  $R^{21}$  representing a hydrogen atom, an alkyl radical or an aralkyl radical the aryl group of which is optionally substituted 1 to 3 times by substituents chosen independently from the group constituted by a halogen atom, an alkyl radical, a haloalkyl radical, an alkoxy radical, a haloalkoxy radical, a hydroxy radical, a nitro radical, a cyano radical, the phenyl radical, an  $SO_2NHR^{29}$  radical and an  $NR^{30}R^{31}$  radical,  $R^{29}$  representing a hydrogen atom or an alkyl or phenyl radical, and  $R^{30}$  and  $R^{31}$  independently representing alkyl radicals,  
25  $R^{22}$  representing a hydrogen atom or an alkyl radical,  
or also  $R^{21}$  and  $R^{22}$  forming together with the nitrogen atom a heterocycle with 4 to 7 members comprising 1 to 2 heteroatoms, the members necessary to complete the heterocycle being chosen independently from the  $-CR^{32}R^{33}$ -,  $-O-$ ,  $-S-$  and  
30  $-NR^{34}-$  radicals,  $R^{32}$  and  $R^{33}$  independently representing each time that they occur a hydrogen atom or an alkyl radical, and  $R^{34}$  representing a hydrogen atom, an alkyl or aralkyl radical, or also  $R^{34}$  representing a phenyl radical optionally substituted 1 to 3 times by substituents chosen independently from a halogen atom and an alkyl or alkoxy radical,  
35  $R^{37}$  and  $R^{38}$  being chosen independently from a hydrogen atom and an alkyl radical or  $R^{37}$  and  $R^{38}$  forming together with the nitrogen atom a heterocycle with 4 to 7 members comprising 1 to 2 heteroatoms, the members necessary to complete the heterocycle

being chosen independently from the  $-CR^{39}R^{40}$ ,  $-O-$ ,  $-S-$  and  $-NR^{41}-$  radicals,  $R^{39}$  and  $R^{40}$  independently representing each time that they occur a hydrogen atom or an alkyl radical, and  $R^{41}$  representing a hydrogen atom or an alkyl radical; and

5 W represents O or S;

or a pharmaceutically acceptable salt of a compound of general formula (I).

3. Product according to claim 2, characterized in that the compound of general formula (I) or its pharmaceutically acceptable salt is chosen from the following compounds:

- 5-{{2-(dimethylamino)ethyl}amino}-2-methyl-1,3-benzothiazole-4,7-dione;

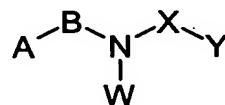
10 - 2-methyl-5-[(2-pyrrolidin-1-ylethyl)amino]-1,3-benzothiazole-4,7-dione;

- 2-methyl-5-[(2-piperidin-1-ylethyl)amino]-1,3-benzothiazole-4,7-dione;

- 2-(2-chloro-6-fluorophenyl)-5-{{2-(dimethylamino)ethyl}amino}-1,3-benzothiazole-4,7-dione;

and the pharmaceutically acceptable salts of the latter.

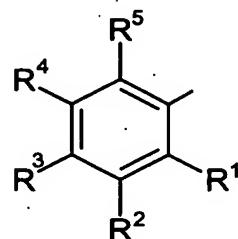
15 4. Product according to claim 1, characterized in that the Cdc25 phosphatase inhibitor combined with the other anti-cancer agent is a compound of general formula (II)



(II)

in which:

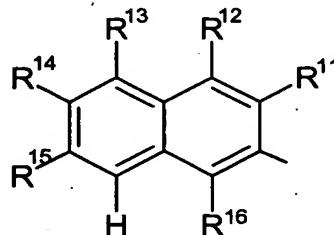
A represents an (A1) radical



(A1)

in which two of the R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup> and R<sup>5</sup> groups represent hydrogen atoms and the other three are chosen independently from a hydrogen atom, a halogen atom and an alkyl, hydroxy, alkoxy, alkylcarbonyloxy, alkylthio or NR<sup>6</sup>R<sup>7</sup> radical, it being understood moreover that:

- 5 - either R<sup>1</sup> and one of R<sup>2</sup> and R<sup>4</sup> are chosen independently from a hydroxy, alkylcarbonyloxy and NR<sup>6</sup>R<sup>7</sup> radical,
- or R<sup>2</sup> and one of R<sup>3</sup> and R<sup>5</sup> are chosen independently from a hydroxy, alkylcarbonyloxy and NR<sup>6</sup>R<sup>7</sup> radical,
- or R<sup>4</sup> and one of R<sup>3</sup> and R<sup>5</sup> are chosen independently from a hydroxy, alkylcarbonyloxy and NR<sup>6</sup>R<sup>7</sup> radical,
- 10 - or also one of R<sup>1</sup>, R<sup>3</sup> and R<sup>5</sup> is chosen from a hydroxy, alkylcarbonyloxy and NR<sup>6</sup>R<sup>7</sup> radical, and the remainder B-N(W)-X-Y is attached to the A radical by a nitrogen atom, R<sup>6</sup> and R<sup>7</sup> representing, independently each time that they occur, a hydrogen atom or an alkyl radical or R<sup>6</sup> and R<sup>7</sup> forming together with the nitrogen atom a heterocycle with 4 to 7 members comprising 1 to 2 heteroatoms, the members necessary to complete the heterocycle being chosen independently from the -CR<sup>8</sup>R<sup>9</sup>-, -O-, -S- and -NR<sup>10</sup>- radicals, R<sup>8</sup> and R<sup>9</sup> independently representing each time that they occur a hydrogen atom or an alkyl, alkoxy, benzyloxycarbonylamino or dialkylamino radical, and R<sup>10</sup> independently representing each time that it occurs a hydrogen atom or an alkyl radical,
- 15
- 20 or also A represents an (A2) radical



(A2)

in which:

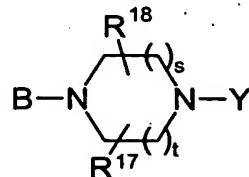
- either R<sup>11</sup> and one of R<sup>13</sup>, R<sup>14</sup> and R<sup>15</sup> represent hydroxy radicals while the other radicals from R<sup>13</sup>, R<sup>14</sup> and R<sup>15</sup> as well as R<sup>16</sup> represent hydrogen atoms,
- or R<sup>12</sup> and R<sup>16</sup> represent hydroxy radicals while R<sup>11</sup>, R<sup>13</sup>, R<sup>14</sup> and R<sup>15</sup> represent hydrogen atoms;
- 25

B represents a -CO-, -NH-CO-(CH<sub>2</sub>)<sub>n</sub>- or -(CH<sub>2</sub>)<sub>p</sub>- radical, n being an integer from 0 to 3 and p being an integer from 0 to 1;

W represents a hydrogen atom or an alkyl radical;

X represents a  $-(CH_2)_q-$ ,  $-(CH_2)_q-NH-$  or  $-CO-(CH_2)_r-$  radical, q being an integer from 1 to 6 and r an integer from 0 to 6;

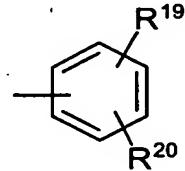
or also the B-N(W)-X-Y group is such that it represents the radical



5 in which B is as defined above, t is an integer from 0 to 2, s is an integer from 0 to 1 and R<sup>17</sup> and R<sup>18</sup> represent radicals chosen independently from a hydrogen atom and an alkyl radical;

and:

- when X represents a  $-(CH_2)_q-$  or  $-CO-(CH_2)_r-$  radical, then Y represents a radical



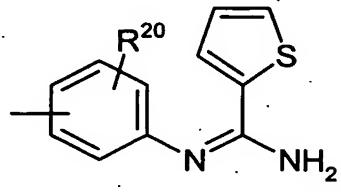
10 in which R<sup>19</sup> represents a hydrogen atom, a halogen atom, a nitro, alkyl, alkylthio, NR<sup>21</sup>R<sup>22</sup>, -SO<sub>2</sub>-NR<sup>23</sup>R<sup>24</sup>, -NH-SO<sub>2</sub>-R<sup>25</sup> or -O-P(O)(OR<sup>26</sup>)(OR<sup>27</sup>) radical, R<sup>21</sup> and R<sup>22</sup> independently representing a hydrogen atom or an alkyl radical, R<sup>23</sup> and R<sup>24</sup> independently representing a hydrogen atom or an alkyl radical, or R<sup>23</sup> and R<sup>24</sup> representing together with the nitrogen atom which carries them a heterocycle with 5 to 7 members the complimentary members of which are chosen independently from -CHR<sup>28</sup>-, -NR<sup>29</sup>-, -O- and -S-, R<sup>28</sup> and R<sup>29</sup> representing, independently each time that they occur, a hydrogen atom or an alkyl radical,

15 R<sup>25</sup> representing an alkyl, haloalkyl radical or one of the aryl, heteroaryl, aralkyl or heteroaralkyl radicals the aryl or heteroaryl nucleus of which is optionally substituted by one or more radicals chosen independently from a halogen atom and alkyl, haloalkyl, hydroxy, alkoxy or nitro radicals, except for the optional nitrogen atoms of the heteroaryl nucleus the optional substituents of which are chosen from alkyl radicals,

20 R<sup>26</sup> and R<sup>27</sup> being chosen independently from alkyl radicals,

and  $R^{20}$  represents a hydrogen atom, a halogen atom or an alkyl, alkoxy or alkylthio radical,

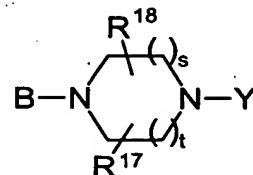
or also Y represents the (T) radical represented below



(T)

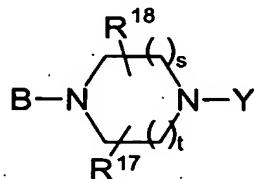
in which  $R^{20}$  represents a hydrogen atom or an alkyl, alkoxy or alkylthio radical,

5 - when X represents a  $-(CH_2)_q-NH-$  radical or when the B-N(W)-X-Y group is such that it represents the radical



then Y represents exclusively an  $-SO_2-R^{30}$  radical in which  $R^{30}$  represents an alkyl, haloalkyl radical or one of the aryl, heteroaryl, aralkyl or heteroaralkyl radicals the aryl or heteroaryl nucleus of which is optionally substituted by one or more radicals chosen independently from a halogen atom and alkyl, haloalkyl, hydroxy, alkoxy or nitro radicals, except for the optional nitrogen atoms of the heteroaryl nucleus the optional substituents of which are chosen from alkyl radicals;

it being understood moreover that when the B-N(W)-X-Y group is such that it represents the radical



15 then B represents exclusively a  $-CO-$  or  $-(CH_2)-$  radical;

or a pharmaceutically acceptable salt of such a compound.

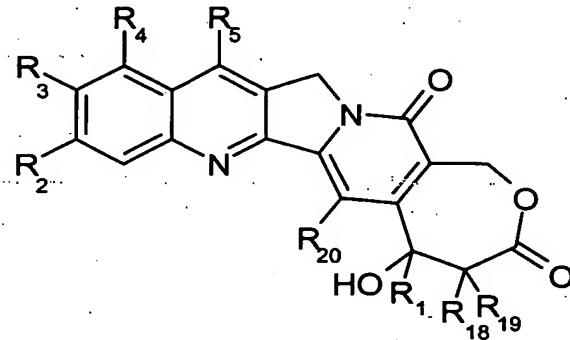
5. Product according to claim 1, characterized in that the Cdc25 phosphatase inhibitor combined with the other anti-cancer agent is chosen from menadione and its analogues.

6. Product according to one of claims 1 to 5, characterized in that the anti-cancer agent combined with the Cdc25 phosphatase inhibitor is chosen from analogues of DNA bases, type I and/or II topoisomerase inhibitors, compounds interacting with the cell spindle, compounds acting on the cytoskeleton, inhibitors of the transduction of the signal passing through the heterotrimeric G proteins, prenyltransferase inhibitors, cyclin-dependent kinase (CDKs) inhibitors, alkylating agents and inhibitors of DNA synthesis and cell division.

10 7. Product according to claim 6, characterized in that the anti-cancer agent combined with the Cdc25 phosphatase inhibitor is a type I and/or II topoisomerase inhibitor.

8. Product according to claim 7, characterized in that the type I and/or II topoisomerase inhibitor is camptothecin or one of its analogues.

15 9. Product according to claim 8, characterized in that the type I and/or II topoisomerase inhibitor is a compound of general formula (III)



in racemic, enantiomeric form or all combinations of these forms, in which

R<sub>1</sub> represents a lower alkyl, a lower alkenyl, a lower alkynyl, a lower haloalkyl, a lower alkoxy lower alkyl or a lower alkylthio lower alkyl;

20 R<sub>2</sub>, R<sub>3</sub> and R<sub>4</sub> represent, independently, i) H, halo, lower halo alkyl, lower alkyl, lower alkenyl, cyano, lower cyano alkyl, nitro, lower nitro alkyl, amido, lower amido alkyl, hydrazino, lower hydrazino alkyl, azido, lower azido alkyl, (CH<sub>2</sub>)<sub>m</sub>NR<sub>6</sub>R<sub>7</sub>, (CH<sub>2</sub>)<sub>m</sub>OR<sub>6</sub>, (CH<sub>2</sub>)<sub>m</sub>SR<sub>6</sub>, (CH<sub>2</sub>)<sub>m</sub>CO<sub>2</sub>R<sub>6</sub>, (CH<sub>2</sub>)<sub>m</sub>NR<sub>6</sub>C(O)R<sub>8</sub>, (CH<sub>2</sub>)<sub>m</sub>C(O)R<sub>8</sub>, (CH<sub>2</sub>)<sub>m</sub>OC(O)R<sub>8</sub>, O(CH<sub>2</sub>)<sub>m</sub>NR<sub>6</sub>R<sub>7</sub>, OC(O)NR<sub>6</sub>R<sub>7</sub>, OC(O)(CH<sub>2</sub>)<sub>m</sub>CO<sub>2</sub>R<sub>6</sub>, or ii) the following radicals substituted (i.e., substituted one to four times on the

aryl group or the heterocycle) or not substituted:  $(CH_2)_n[N=X]$ ,  $OC(O)[N=X]$ ,  $(CH_2)_mOC(O)[N=X]$  (in which  $[N=X]$ , in this invention, represents a heterocyclic group with 4 to 7 members with the nitrogen atom N, which is a member of the heterocyclic group, and X represents the remaining members, necessary to complete the heterocyclic group, selected from the group constituted by O, S,  $CH_2$ ,  $CH$ , N,  $NR_9$  and  $COR_{10}$ ), aryl or lower aryl alkyl, in which the optional substituents are chosen from the group constituted by a lower alkyl, halo, nitro, amino, lower alkylamino, lower haloalkyl, lower hydroxy alkyl, lower alkoxy, and lower alkoxy lower alkyl; or  $R_2$  and  $R_3$  together form a chain with 3 or 4 members, in which the elements of the chain are selected from the group constituted by  $CH$ ,  $CH_2$ , O, S, N or  $NR_9$ ;

$R_5$  represents i) H, halo, lower halo alkyl, lower alkyl, lower alkoxy, lower alkoxy lower alkyl, lower alkylthio lower alkyl, cycloalkyl, lower cycloalkyl alkyl, cyano, cyano alkyl, lower alkyl lower sulphonyl alkyl, lower hydroxy alkyl, nitro,  $(CH_2)_mC(O)R_8$ ,  $(CH_2)_mNR_6C(O)R_8$ ,  $(CH_2)_mNR_6R_7$ ,  $(CH_2)_mN(CH_3)(CH_2)_nNR_6R_7$ ,  $(CH_2)_mOC(O)R_8$ ,  $(CH_2)_mOC(O)NR_6R_7$ ,  $(CH_2)_mS(O)_qR_{11}$ ,  $(CH_2)_mP(O)R_{12}R_{13}$ ,  $(CH_2)_2P(S)R_{12}R_{13}$ , or ii) one of the following radicals substituted (i.e. one to four times on the aryl or heteroaryl group) or not substituted:  $(CH_2)_n[N=X]$ ,  $OC(O)[N=X]$ ,  $(CH_2)_mOC(O)[N=X]$ , aryl or lower aryl alkyl, in which the optional substituents are chosen from the group constituted by a lower alkyl, halo, nitro, amino, lower alkyl amino, lower halo alkyl, lower hydroxy alkyl, lower alkoxy and lower alkoxy lower alkyl;

$R_6$  and  $R_7$  represent, independently, i) H, a lower alkyl, lower hydroxy alkyl, lower alkyl lower amino alkyl, lower amino alkyl, cycloalkyl, lower cycloalkyl alkyl, lower alkenyl, lower alkoxy lower alkyl, lower halo alkyl, or ii) one of the following radicals substituted (i.e., one to four times on the aryl group) or not substituted: aryl or lower aryl alkyl, in which the optional substituents are chosen from the group constituted by a lower alkyl, halo, nitro, amino, lower alkyl amino, lower halo alkyl, lower hydroxy alkyl, lower alkoxy, and lower alkoxy lower alkyl;

$R_8$  represents i) H, a lower alkyl, lower hydroxy alkyl, amino, lower alkyl amino, lower alkyl amino lower alkyl, lower amino alkyl, cycloalkyl, lower cycloalkyl alkyl, lower alkenyl, lower alkoxy, lower alkoxy lower alkyl, lower halo alkyl, or ii) one of the following radicals substituted (i.e., one to four times on the aryl group) or not substituted: aryl or lower

aryl alkyl, in which the optional substituents are chosen from the group constituted by a lower alkyl, halo, nitro, amino, lower alkyl amino, lower halo alkyl, lower hydroxy alkyl, lower alkoxy, or lower alkoxy lower alkyl;

5 R<sub>9</sub> represents H, a lower alkyl, lower halo alkyl, aryl, or aryl substituted by one or more groups chosen from the lower alkyl radical, halo, nitro, amino, lower alkyl amino, lower halo alkyl, lower hydroxy alkyl, lower alkoxy, or lower alkoxy lower alkyl;

10 R<sub>10</sub> represents H, a lower alkyl, lower halo alkyl, lower alkoxy, aryl, or aryl substituted (i.e., presenting one to four substituents on the aryl group) by one or more groups chosen from the lower alkyl radical, lower halo alkyl, lower hydroxy alkyl, or lower alkoxy lower alkyl;

R<sub>11</sub> represents a lower alkyl, aryl,  $(CH_2)_mOR_{14}$ ,  $(CH_2)_mSR_{14}$ ,  $(CH_2)_2NR_{14}R_{15}$  or  $(CH_2)_m[N=X]$ ;

15 R<sub>12</sub> and R<sub>13</sub> representing, independently, a lower alkyl, aryl, lower alkoxy, aryloxy or amino;

R<sub>14</sub> and R<sub>15</sub> representing, independently, H, a lower alkyl or aryl;

R<sub>18</sub> and R<sub>19</sub> representing, independently, H, halo, lower alkyl, lower alkoxy or hydroxy;

20 R<sub>20</sub> represents H or halo;

m is a whole number comprised between 0 and 6;

n is 1 or 2; and

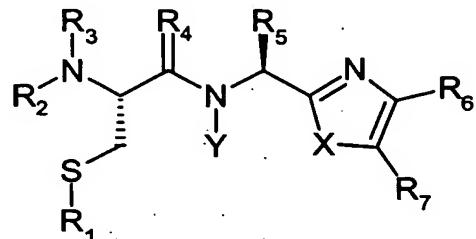
q represents a whole number from 0 to 2; and [N=X] represents a heterocyclic group with 4 to 7 members, X representing the chain necessary to complete said heterocyclic group and selected from the group constituted by O, S, CH<sub>2</sub>, CH, N, NR<sub>9</sub> and COR<sub>10</sub>;

25 or a pharmaceutically acceptable salt of the latter.

10. Product according to claim 9, characterized in that the compound of general formula (III) or its pharmaceutically acceptable salt is chosen from diflomotecan and (+)-9-chloro-5-ethyl-5-hydroxy-10-methyl-12-(4-methylpiperidinomethyl)-4,5,13,15-tetrahydro-1H,3H-oxepino[3',4':6,7]indolizino[1,2-c]quinoline-3,15-dione and its pharmaceutically acceptable salts.

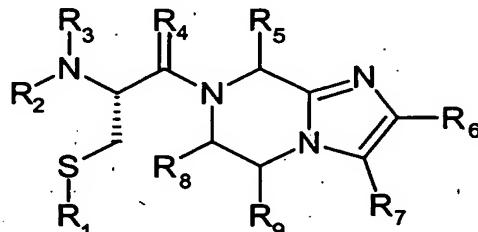
11. Product according to claim 6, characterized in that the anti-cancer agent combined with the Cdc25 phosphatase inhibitor is an inhibitor of the transduction of the signal passing through the heterotrimeric G proteins.

12. Product according to claim 11, characterized in that the inhibitor of the transduction of the signal passing through the heterotrimeric G proteins is chosen from the compounds of general formula (IV)

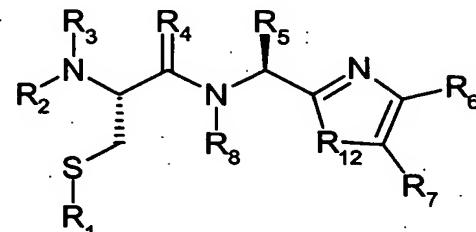


(IV)

corresponding to the sub-formulae (IV<sub>A</sub>) or (IV<sub>B</sub>):



(IVA)



(IVB)

5 in which:

X represents R<sub>12</sub> and Y represents R<sub>8</sub>, or X and Y complete a ring with 6 members, the X-Y group representing the -CH(R<sub>8</sub>)-CH(R<sub>9</sub>)- radical;

R<sub>1</sub> represents H, an alkyl, alkylthio or cycloalkylthio radical;

R<sub>2</sub> and R<sub>3</sub> independently represent H or an alkyl or cycloalkyl radical;

10 R<sub>4</sub> represents H<sub>2</sub> or O;

R<sub>5</sub> represents H, or one of the alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, aralkyl, heterocyclyl or heterocyclylalkyl radicals, these radicals being optionally substituted by radicals chosen from the group comprising an alkyl, -O-R<sub>10</sub>, -S(O)<sub>m</sub>R<sub>10</sub> (m representing 0, 1, or 2), -N(R<sub>10</sub>)(R<sub>11</sub>), -N-C(O)-R<sub>10</sub>,

15 -NH-(SO<sub>2</sub>)-R<sub>10</sub>, -CO<sub>2</sub>-R<sub>10</sub>, -C(O)-N(R<sub>10</sub>)(R<sub>11</sub>), and -(SO<sub>2</sub>)-N(R<sub>10</sub>)(R<sub>11</sub>) radical;

R<sub>6</sub> and R<sub>7</sub> independently represent H, a -C(O)-NH-CHR<sub>13</sub>-CO<sub>2</sub>R<sub>14</sub> radical, or one of the alkyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, aralkyl, heterocyclyl or heterocyclylalkyl radicals, these radicals being optionally substituted by

radicals chosen from the group comprising the OH, alkyl or alkoxy, N(R<sub>10</sub>)(R<sub>11</sub>), COOH, CON(R<sub>10</sub>)(R<sub>11</sub>), and halo radicals,

or R<sub>6</sub> and R<sub>7</sub> together form an aryl radical or a heterocycle;

5 R<sub>8</sub> and R<sub>9</sub> independently represent, H, or one of the alkyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, aralkyl, heterocyclyl or heterocyclylalkyl radicals, these radicals being optionally substituted by radicals chosen from the group comprising the OH, alkyl or alkoxy, N(R<sub>10</sub>)(R<sub>11</sub>), COOH, CON(R<sub>10</sub>)(R<sub>11</sub>) and halo radicals,

or R<sub>8</sub> and R<sub>9</sub> together form an aryl radical or a heterocycle;

10 R<sub>10</sub> and R<sub>11</sub>, independently represent H, an aryl radical or heterocyclyl, or an alkyl, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl or heterocyclylalkyl radical;

R<sub>12</sub> represents NR<sub>9</sub>, S, or O;

R<sub>13</sub> represents an alkyl radical optionally substituted by a radical chosen from the alkyl, -OR<sub>10</sub>, -S(O)<sub>m</sub>R<sub>10</sub> (m representing 0, 1, or 2) and -N(R<sub>10</sub>)(R<sub>11</sub>) radicals;

R<sub>14</sub> represents H or an alkyl radical;

15 and the pharmaceutically acceptable salts of the latter.

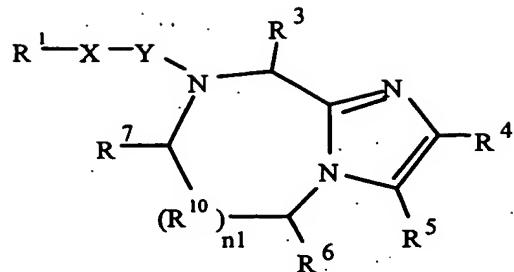
13. Product according to claim 12, characterized in that the compound of general formula (IV) or its pharmaceutically acceptable salt is chosen from 7-(2-amino-1-oxo-3-thiopropyl)-8-(cyclohexylmethyl)-2-phenyl-5,6,7,8-tetrahydroimidazo[1,2a]pyrazine and its dimer form, bis-1,1'-{7-(2-amino-1-oxo-3-thiopropyl)-8-(cyclohexylmethyl)-2-phenyl-5,6,7,8-tetrahydroimidazo[1,2a]pyrazine}disulphide or (1R)-1-[(2R)-2-amino-3-[(8S)-8-(cyclohexylmethyl)-2-phenyl-5,6-dihydroimidazo[1,2-a]pyrazin-7(8H)-yl]-3-oxopropyl]dithio)methyl]-2-[(8S)-8-(cyclohexylmethyl)-2-phenyl-5,6-dihydroimidazo[1,2-a]pyrazin-7(8H)-yl]-2-oxoethylamine, and the pharmaceutically acceptable salts of these compounds.

25 14. Product according to claim 6, characterized in that the anti-cancer agent combined with the Cdc25 phosphatases inhibitor is a prenyltransferase inhibitor.

15. Product according to claim 14, characterized in that the prenyltransferase inhibitor is a farnesyltransferase inhibitor.

30 16. Product according to claim 15, characterized in that the farnesyltransferase inhibitor is chosen from the group comprised:

- of a compound of general formula (V)



(V)

in which:

n1 represents 0 or 1;

X represents, independently each time that it occurs,  $(CH_2)_nZ(CH_2)_m$ ;

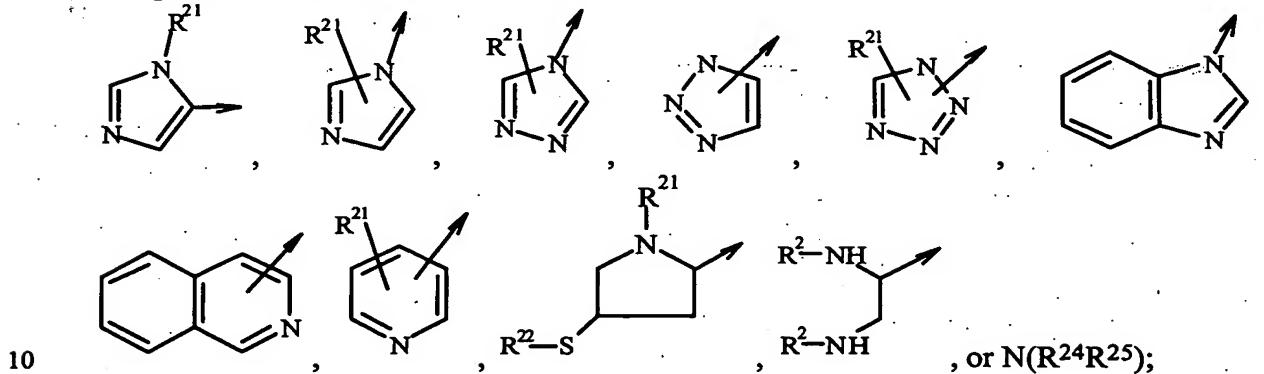
Z representing O, N( $R^{12}$ ), S, or a bond;

5 n3 representing, independently each time that it occurs, 0 or 1;

each of  $n_4$  and  $n_5$  representing, independently each time that they occurs, 0, 1, 2, or 3;

Y represents, independently each time that it occurs, CO, CH<sub>2</sub>, CS, or a bond;

**R<sup>1</sup>** represents one of the radicals



each of  $R^2$ ,  $R^{11}$ , and  $R^{12}$  representing, independently each time that it occurs, H or an optionally substituted radical chosen from the group consisting of a ( $C_{1-6}$ )alkyl radical and an aryl radical, said optionally substituted radical being optionally substituted by at least one radical chosen from the  $R^8$  and  $R^{30}$  radicals, each substituent being chosen independently of the others;

$R^3$  represents, independently each time that it occurs, H or an optionally substituted radical chosen from the group consisting of the  $(C_{1-6})alkyl$ ,  $(C_{2-6})alkenyl$ ,  $(C_{2-6})alkynyl$ ,

(C<sub>3-6</sub>)cycloalkyl, (C<sub>3-6</sub>)cycloalkyl(C<sub>1-6</sub>)alkyl, (C<sub>5-7</sub>)cycloalkenyl, (C<sub>5-7</sub>)cycloalkenyl(C<sub>1-6</sub>)alkyl, aryl, aryl(C<sub>1-6</sub>)alkyl, heterocyclyl, and heterocyclyl(C<sub>1-6</sub>)alkyl radicals, said optionally substituted radical being optionally substituted by at least one radical chosen from the R<sup>30</sup> radicals, each substituent being chosen independently of the others;

5 each of R<sup>4</sup> and R<sup>5</sup> represents, independently each time that it occurs, H or an optionally substituted radical chosen from the group consisting of the (C<sub>1-6</sub>)alkyl, (C<sub>3-6</sub>)cycloalkyl, aryl and heterocyclyl radicals, said optionally substituted radical being optionally substituted by at least one radical chosen from the R<sup>30</sup> radicals, each substituent being chosen independently of the others, or R<sup>4</sup> and R<sup>5</sup> taken together with the carbon atoms to which they are attached together form an aryl radical;

10 R<sup>6</sup> represents, independently each time that it occurs, H or an optionally substituted radical chosen from the group consisting of the (C<sub>1-6</sub>)alkyl, (C<sub>2-6</sub>)alkenyl, (C<sub>3-6</sub>)cycloalkyl, (C<sub>3-6</sub>)cycloalkyl(C<sub>1-6</sub>)alkyl, (C<sub>5-7</sub>)cycloalkenyl, (C<sub>5-7</sub>)cycloalkenyl(C<sub>1-6</sub>)alkyl, aryl, aryl(C<sub>1-6</sub>)alkyl, heterocyclyl and heterocyclyl(C<sub>1-6</sub>)alkyl radicals, said 15 optionally substituted radical being optionally substituted by at least one radical chosen from the OH, (C<sub>1-6</sub>)alkyl, (C<sub>1-6</sub>)alkoxy, -N(R<sup>8</sup>R<sup>9</sup>), -COOH, -CON(R<sup>8</sup>R<sup>9</sup>) and halo radicals, each substituent being chosen independently of the others;

20 R<sup>7</sup> represents, independently each time that it occurs, H, =O, =S, H or an optionally substituted radical chosen from the group consisting of the (C<sub>1-6</sub>)alkyl, (C<sub>2-6</sub>)alkenyl, (C<sub>3-6</sub>)cycloalkyl, (C<sub>3-6</sub>)cycloalkyl(C<sub>1-6</sub>)alkyl, (C<sub>5-7</sub>)cycloalkenyl, (C<sub>5-7</sub>)cycloalkenyl(C<sub>1-6</sub>)alkyl, aryl, aryl(C<sub>1-6</sub>)alkyl, heterocyclyl and heterocyclyl(C<sub>1-6</sub>)alkyl radicals, said 25 optionally substituted radical being optionally substituted by at least one radical chosen from the OH, (C<sub>1-6</sub>)alkyl, (C<sub>1-6</sub>)alkoxy, -N(R<sup>8</sup>R<sup>9</sup>), -COOH, -CON(R<sup>8</sup>R<sup>9</sup>) and halo radicals, each substituent being chosen independently of the others;

each of R<sup>8</sup> and R<sup>9</sup> representing, independently each time that it occurs, H, (C<sub>1-6</sub>)alkyl, (C<sub>2-6</sub>)alkenyl, (C<sub>2-6</sub>)alkynyl, aryl, or aryl(C<sub>1-6</sub>)alkyl;

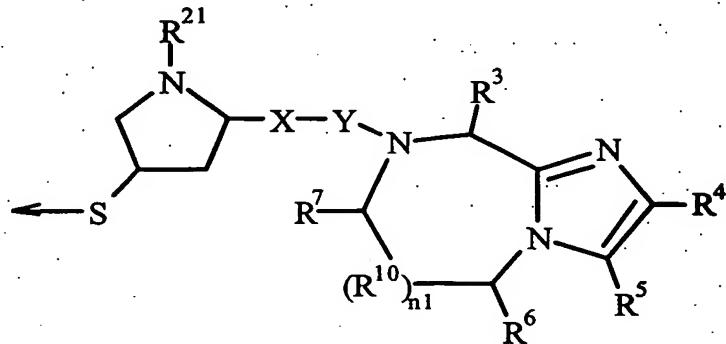
R<sup>10</sup> represents C;

30 or, when n<sub>1</sub> = 0, R<sup>6</sup> and R<sup>7</sup> can be taken together with the carbon atoms to which they are attached to form an aryl radical or cyclohexyl;

R<sup>21</sup> represents, independently each time that it occurs, H or an optionally substituted radical chosen from the group consisting of the (C<sub>1-6</sub>)alkyl and aryl(C<sub>1-6</sub>)alkyl radicals, said optionally substituted radical being optionally substituted by at least one radical

chosen from the  $R^8$  and  $R^{30}$  radicals, each substituent being chosen independently of the others;

$R^{22}$  represents H, ( $C_{1-6}$ )alkylthio, ( $C_{3-6}$ )cycloalkylthio,  $R^8-CO-$ , or a substituent of formula



5 each of  $R^{24}$  and  $R^{25}$  represents, independently each time that it occurs, H, ( $C_{1-6}$ )alkyl or aryl( $C_{1-6}$ )alkyl;

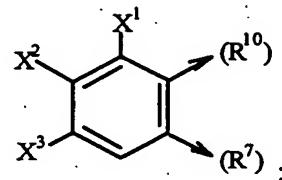
$R^{30}$  represents, independently each time that it occurs, ( $C_{1-6}$ )alkyl,  $-O-R^8$ ,  $-S(O)_{n6}R^8$ ,  $-S(O)_{n7}N(R^8R^9)$ ,  $-N(R^8R^9)$ ,  $-CN$ ,  $-NO_2$ ,  $-CO_2R^8$ ,  $-CON(R^8R^9)$ ,  $-NCO-R^8$ , or halogen, each of  $n6$  and  $n7$  representing, independently each time that it occurs, 0, 1 or 2;

10 said heterocyclyl radical being azepinyl, benzimidazolyl, benzisoxazolyl, benzofurazanyl, benzopyranyl, benzothiopyranyl, benzofuryl, benzothiazolyl, benzothienyl, benzoxazolyl, chromanyl, cinnolinyl, dihydrobenzofuryl, dihydrobenzothienyl, dihydrobenzothiopyranyl, dihydrobenzothio-pyranyl sulphone, furyl, imidazolidinyl, imidazolinyl, imidazolyl, indolinyl, indolyl, isochromanyl, 15 isoindolinyl, isoquinolinyl, isothiazolidinyl, isothiazolyl, isothiazolidinyl, morpholinyl, naphthyridinyl, oxadiazolyl, 2-oxoazepinyl, 2-oxopiperazinyl, 2-oxopiperidinyl, 2-oxopyrrolidinyl, piperidyl, piperazinyl, pyridyl, pyridyl-N-oxide, quinoxaliny, tetrahydrofuryl, tetrahydroisoquinolinyl, tetrahydro-quinolinyl, thiamorpholinyl, thiamorpholinyl sulphoxide, thiazolyl, thiazolinyl, thienofuryl, thienothienyl or thienyl;

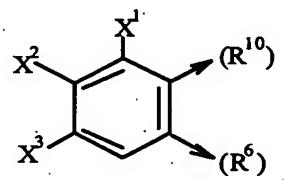
20 said radical aryl being phenyl or naphthyl;

it being understood that:

when  $n_1 = 1$ ,  $R^{10}$  is C and  $R^6$  represents H, then  $R^{10}$  and  $R^7$  can form, taken together, the radical

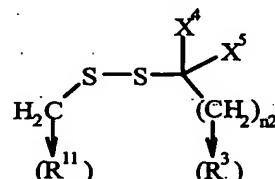


or when  $n_1 = 1$ ,  $R^{10}$  is C, and  $R^7$  is =O, -H, or =S, then  $R^{10}$  and  $R^6$  can form, taken together, the radical



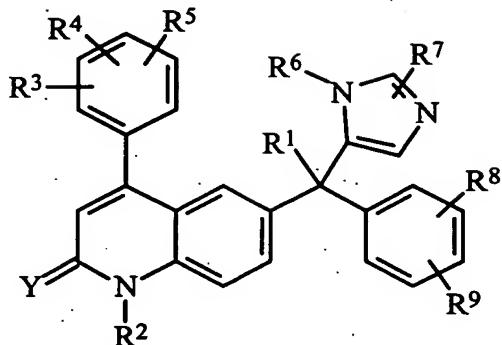
5. with each of  $X^1$ ,  $X^2$ , and  $X^3$  representing, independently, H, a halogen atom,  $-NO_2$ ,  $-NCO-R^8$ ,  $-CO_2R^8$ ,  $-CN$ , or  $-CON(R^8R^9)$ ; and

when  $R^1$  is  $N(R^{24}R^{25})$ , then  $n_3$  represents 1, each of  $n_4$  and  $n_5$  represents 0,  $Z$  is a bond, and  $R^3$  and  $R^{11}$  can form, taken together, the radical



10 with  $n_2$  representing an integer from 1 to 6, and each of  $X^4$  and  $X^5$  representing, independently, H,  $(C_{1-6})$ alkyl or aryl, or  $X^4$  and  $X^5$  forming, taken together, a  $(C_{3-6})$ cycloalkyl radical;

- of a compound of general formula (VI)



(VI)

in which:

R<sup>1</sup> represents H or an alkyl, OR<sup>10</sup>, SR<sup>10</sup> or NR<sup>11</sup>R<sup>12</sup> radical;

R<sup>2</sup> represents H or an alkyl radical;

5 R<sup>3</sup>, R<sup>4</sup> and R<sup>5</sup> represent, independently, H, a halogen atom or an alkyl, trihalomethyl, hydroxy, cyano or alkoxy radical;

R<sup>6</sup> represents H or an alkyl radical;

R<sup>7</sup> represents H, a halogen atom or an alkyl, hydroxyalkyl, amino, hydroxycarbonyl radical;

10 R<sup>8</sup> and R<sup>9</sup> represent, independently, H, a halogen atom or a cyano, alkyl, trihalomethyl, alkoxy, alkylthio or dialkylamino radical;

R<sup>10</sup> represents H or an alkyl or alkylcarbonyl radical;

R<sup>11</sup> represents H or an alkyl radical;

R<sup>12</sup> represents H or an alkyl or alkylcarbonyl radical;

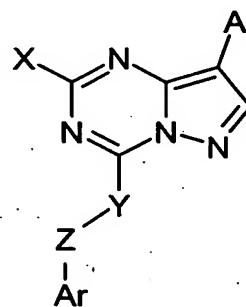
15 and Y represents O or S;

- and a pharmaceutically acceptable salt of a compound of general formula (V) or of a compound of general formula (VI).

17. Product according to claim 16, characterized in that the farnesyltransferase inhibitor is 1-(2-(1-((4-cyano)phenylmethyl)imidazol-4-yl)-1-oxoethyl-2,5-dihydro-4-(2-methoxyphenyl)imidazo[1,2c][1,4]benzodiazepine, 4-(2-bromophenyl)-1-(2-(1-((4-cyano-3-methoxy)phenylmethyl)imidazo-5-yl)-5-1-oxoethyl)-1,2-dihydro-8-fluoroimidazol[1,2a][1,4]-benzodiazepine or one of its pharmaceutically acceptable salts.

18. Product according to claim 6, characterized in that the anti-cancer agent combined with the Cdc25 phosphatase inhibitor is a cyclin-dependent kinase (CDK) inhibitor.

19. Product according to claim 18, characterized in that the CDK inhibitor is chosen from the compounds of general formula (VII)



(VII)

in racemic, enantiomeric form or all combination of these forms, in which

A represents a hydrogen atom, a halogen atom, a formyl, cyano, nitro, guanidinoaminomethylenyl, (1,3-dihydro-2-oxoindol)-3-ylidenemethyl, alkylcarbonyl, aralkylcarbonyl or heteroaralkylcarbonyl radical, or also a 15 -L-NR<sup>1</sup>R<sup>2</sup> radical in which L represents an alkylene radical and R<sup>1</sup> and R<sup>2</sup> are chosen independently from a hydrogen atom and an alkyl radical or R<sup>1</sup> and R<sup>2</sup> taken together with the nitrogen atom which carries them form a heterocycle with 5 to 7 members, the complimentary members being chosen independently from the group comprising -CH<sub>2</sub>-, -NR<sup>3</sup>-, -S- and -O-, R<sup>3</sup> independently representing each time that it occurs a hydrogen atom or an alkyl radical;

X represents a hydrogen atom, an alkylthio, aralkylthio, alkylthioxo or aralkylthioxo radical, or also an NR<sup>4</sup>R<sup>5</sup> radical in which R<sup>4</sup> represents an alkyl radical, a hydroxyalkyl radical, a cycloalkyl radical optionally substituted by one or more radicals chosen from the alkyl, hydroxy and amino radicals, an aralkyl radical the aryl radical of which is 20 optionally substituted by one or more radicals chosen from a halogen atom, the cyano

radical, the nitro radical and the alkyl or alkoxy radicals, or also R<sup>4</sup> represents a heteroaryl or heteroarylalkyl radical, the heteroaryl radical of the heteroaryl or heteroarylalkyl radicals being optionally substituted by one or more alkyl radicals and R<sup>5</sup> represents a hydrogen atom, or R<sup>4</sup> and R<sup>5</sup> taken together with the nitrogen atom  
5 which carries them form a heterocycle with 5 to 7 members, the complimentary members being chosen independently from the group comprising -CH<sub>2</sub>-, -NR<sup>6</sup>-, -S- and -O-, R<sup>6</sup> independently representing each time that it occurs a hydrogen atom or an alkyl or hydroxyalkyl radical;

Y represents NH or an oxygen atom;

10 Z represents a bond or an alkyl or alkylthioalkyl radical; and

Ar represents a carbocyclic aryl radical optionally substituted 1 to 3 times by radicals chosen independently from a halogen atom, the cyano radical, the nitro radical, an alkyl or alkoxy radical and an NR<sup>7</sup>R<sup>8</sup> radical in which R<sup>7</sup> and R<sup>8</sup> independently represent a hydrogen atom or an alkyl radical or R<sup>7</sup> and R<sup>8</sup> taken together with the nitrogen atom  
15 which carries them form a heterocycle with 5 to 7 members, the complimentary members being chosen independently from the group comprising -CH<sub>2</sub>-, -NR<sup>9</sup>-, -S- and -O-, R<sup>9</sup> independently representing each time that it occurs a hydrogen atom or an alkyl radical,

or also Ar represents a heterocyclic aryl radical having 5 or 6 members and whose heteroatom or heteroatoms are chosen from nitrogen, oxygen or sulphur atoms, said heteroatoms being optionally oxidized (Ar can represent for example the oxidopyridyl radical) and said heterocyclic aryl radical being able to be optionally substituted by one or more radicals chosen independently from the alkyl, aminoalkyl, alkylaminoalkyl and dialkylaminoalkyl radicals;

25 and the pharmaceutically acceptable salts of these compounds.

20. Product according to claim 18, characterized in that the CDK inhibitor is chosen from roscovitine and its analogues.

21. A compound characterized in that it is (1*R*)-1-[(*2R*)-2-amino-3-[(8*S*)-8-(cyclohexylmethyl)-2-phenyl-5,6-dihydroimidazo[1,2-*a*]pyrazin-7(8*H*)-yl]-3-oxopropyl]dithio)methyl]-2-[(8*S*)-8-(cyclohexylmethyl)-2-phenyl-5,6-dihydroimidazo[1,2-*a*]pyrazin-7(8*H*)-yl]-2-oxoethylamine, or a pharmaceutically acceptable salt thereof.

22. A pharmaceutically acceptable salt according to claim 21, characterized in that it is (1*R*)-1-[{({(2*R*)-2-amino-3-[{(8*S*)-8-(cyclohexylmethyl)-2-phenyl-5,6-dihydroimidazo[1,2-*a*]pyrazin-7(8*H*)-yl]-3-oxopropyl}dithio)methyl]-2-[(8*S*)-8-(cyclohexylmethyl)-2-phenyl-5,6-dihydroimidazo[1,2-*a*]pyrazin-7(8*H*)-yl]-2-oxoethylamine tetrahydrochloride.

5

23. A preparation process for making the salt of claim 22, said process being characterized in that it comprises the following steps:

1) reacting approximately 2 equivalents of (8*S*)-8-(cyclohexylmethyl)-2-phenyl-5,6,7,8-tetrahydroimidazo[1,2-*a*]pyrazine with approximately one equivalent of Boc-Cys-Cys-Boc in a polar aprotic solvent; and

10 2) reacting in a lower alcohol the disulphide derivative obtained after stage 1) with an excess of hydrochloric acid in solution in a lower alcohol.